Prevalence and Risk Factors for Chagas Disease in Pregnant Women in Casanare, Colombia

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Abstract. Knowledge of the prevalence and risk factors associated with maternal infection is the first step to develop a surveillance system for congenital transmission of Chagas disease. We conducted a cross-sectional study in Casanare, a disease-endemic area in Colombia. A total of 982 patients were enrolled in the study. A global prevalence of *Trypanosoma cruzi* infection of 4.0% (95% confidence interval [CI] = 2.8-5.3%) was found. Multivariate analysis showed that the most important risk-associated factors were age > 29 years (adjusted odds ratio [aOR] = 3.4, 95% CI = 0.9-12.4), rural residency (aOR = 2.2, 95% CI = 1.0-4.6), low education level (aOR = 10.2, 95% CI = 1.6-82.7), and previous knowledge of the vector (aOR = 2.2, 95% CI = 1.0-4.9). Relatives and siblings of infected mothers showed a prevalence of 9.3%. These findings may help physicians to investigate congenital cases, screen Chagas disease in siblings and relatives, and provide early treatment to prevent the chronic complications of Chagas disease.

INTRODUCTION

Chagas disease, which is caused by the parasite *Trypanosoma cruzi*, continues being a persistent problem in Latin America. It is estimated that 9.8 million persons are infected worldwide. Constant migration from rural to urban areas has lead to urbanization of Chagas disease, and migration of infected persons to other continents has resulted in its globalization. Although transmission by domestic vectors is still the most important route of infection in disease-endemic areas, congenital transmission is the most important transmission route in countries where this disease is not endemic and in urban areas of disease-endemic countries. Consequently, congenital Chagas disease has been reported in countries of North America, Europe, and Asia, with varying prevalence depending on the place of origin of the pregnant women. 2.4-6

In countries where Chagas disease is endemic, it has been estimated that approximately 14,000 new cases of congenital transmission occur annually. The prevalence of Chagas infection in women of childbearing age differs among countries and is dependent on many factors. For instance, in Bolivia it varies from 20% to 60% and in Argentina, Brazil, Chile, Peru, and Paraguay it ranges from 0% to 40%. Likewise, the probability of congenital transmission varies among countries because it is dependent on follow-up time for newborns and diagnostic techniques used, which usually differ from one study to another. One

In Colombia, there are approximately 436,000 infected persons, nearly 5 million persons live in areas at risk for vector-borne domestic transmission, Chagas disease affects closely 130,000 women of childbearing age, and consequently, near 1,000 children with congenital Chagas disease are born annually. Only one study about congenital disease has been conducted in Colombia, in Miraflores and Moniquirá in the department of Boyacá, in the central Andean region. This study reported a prevalence of Chagas disease in pregnant women of 2.7–3.5% and a mother-to-child transmission rate of 20% by hemoculture. 13

In an attempt to obtain knowledge of congenital Chagas disease in Colombia and to promote implementation of routine screening for Chagas disease during the prenatal period, we conducted a study to determine the prevalence of *T. cruzi* infection in pregnant women and its associated risk factors, in the department of Casanare, a disease-endemic area in the Orinoco River Basin region in Colombia.

MATERIALS AND METHODS

Study area. This study was conducted during February-August 2010 in El Yopal, capital of Casanare, a department with 19 municipalities in eastern Colombia, in the region of the Orinoco River Basin between 4°17'25"N and 6°20'45"N and 69°50'22" and 73°4'33"W. The area has an average temperature of 27°C and seasonal variations during the year (Figure 1). In other studies, this department showed a high risk for vector-borne domestic transmission of Chagas disease, mainly by Rhodnius prolixus, Triatoma dimidiata, and T. maculata in all its municipalities. 14 Taking into account that access to some municipalities is difficult, we decided to include all pregnant women at the health centers located in El Yopal where most births and pregnant women from this department receive medical care. The women included in the study were residents of all municipalities of Casanare (Figure 1).

Study design and sampling. This was a cross-sectional study to estimate the prevalence of T. cruzi infection in pregnant women seeking health care at the health centers of El Yopal and to study the epidemiologic factors associated with parasite infection. According to population projections by the Departamento Administrativo Nacional de Estadística of Colombia, the number of expected births in El Yopal in 2010 was 3,144. A global prevalence of $5\% \pm 1.5\%$ was estimated. With a confidence level of 95%, we decided to enroll a minimum of 903 pregnant women in the study. Consequently, all pregnant women who received prenatal control during February–August 2010 at different health centers in El Yopal were requested to participate.

Diagnosis of *T. cruzi* **infection.** Maternal infection was assessed by serologic tests for *T. cruzi* antibodies. The screening technique used to detect IgG to *T. cruzi* was an enzymelinked immunosorbent assay (ELISA) for blood samples

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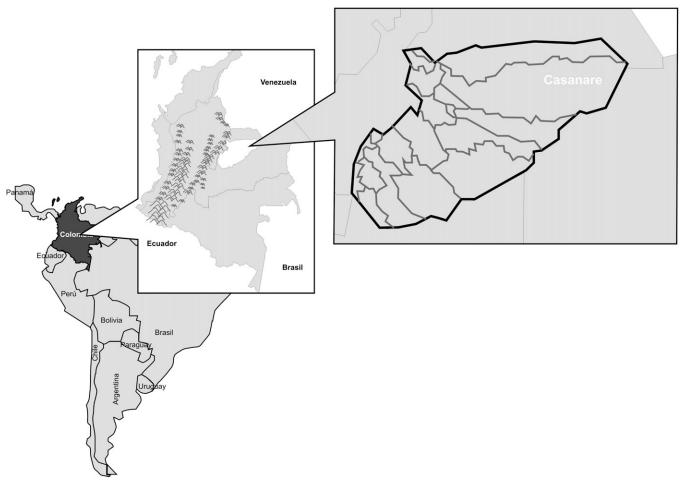


FIGURE 1. Study area in Casanare, Colombia.

placed on filter paper. Positive results were confirmed for serum samples by at least two of the following three tests: ELISA, immunofluorescent assay (IFAT), and indirect hemagglutination assay (IHA). The ELISA and IFAT were standardized by the Grupo de Parasitología at the Instituto Nacional de Salud (Bogotá, Colombia), and the IHA used was obtained from Wiener Laboratories (Rosario, Argentina). The cutoff values were 0.4 for the ELISA on filter paper and 0.3 in serum samples and titers \geq 1:32 and 1:16 for IFAT and IHA, respectively, were considered as reactive. Quality control was conducted by repeating all tests with positive results and 2% of tests with negative results, Concordance was 100%. $^{16-18}$

Questionnaire. A structured interview was conducted by trained personnel to identify the most important factors associated with *T. cruzi* infection. The questionnaire was previously validated in the field by interviews of 30 pregnant women, and questions were adjusted according to this procedure. The survey contained questions about general aspects such as age, socioeconomic stratum, birthplace, place of residence, housing conditions, knowledge or contact with the vector, previous diseases, history of Chagas disease in relatives, specific obstetric history, and current symptoms of Chagas disease.

House visits. To find other relatives infected with *T. cruzi*, and perform house vector control by government trained personnel, visits to the houses of all infected women were conducted.

Statistical analysis. Frequencies were expressed as percentages for qualitative variables and means for the quantitative variables. Absolute and relative frequencies were determined, and univariate and bivariate analyses were conducted by using χ^2 tests. The associations between risk factors and T. cruzi infection in pregnant women were estimated by using odds ratios (OR). A logistic regression was conducted to adjust estimates. Variables in the model were selected by using backward stepwise method and eliminated in an iterative process. 95% confidence intervals (CIs) were calculated and P values ≤ 0.05 were considered significant. Data were analyzed by using STATA version 10.0 (StataCorp LP, College Station, TX). Quality control of database was conducted by using a double-entry process. Identification and some social aspects were compared with those in the database of the Sistema de Identificación de Potenciales Beneficiarios de Programas Sociales of Colombia. 19,20

Ethical aspects. According to national and international standards, this was an investigation that had a minimum risk for patients.^{21,22} The study was approved by the Institutional Review Board of the Instituto Nacional de Salud (approval no. 002, July 11, 2008). Several meetings were held with the pregnant women, in which the objectives and procedures to be followed in the study were explained. All participants signed informed consent forms, and parents or a responsible adult signed the consent form when the women were less than

Table 1
Prevalence of *Trypanosoma cruzi* infection in pregnant women by municipalities of residence, Casanare, Colombia*

	Pregnant women included			Frequency of <i>T. cruzi</i> infection			
Municipality of residence	No.	%	95% CI	No.	%	95% CI	
El Yopal	541	55.1	52.0-58.3	15	2.7	1.6-4.4	
Aguazul	86	8.8	7.1 - 10.8	3	3.5	0.9 - 9.2	
Tauramena	77	7.8	6.3 - 9.8	0	0.0	0.0 - 3.8	
Paz de Ariporo	47	4.8	3.6 - 6.4	1	2.1	0.1 - 10.1	
San Luis de Palenque	41	4.2	3.1 - 5.7	3	7.5	1.9 - 19.1	
Trinidad	44	4.5	3.3 - 6.0	3	6.7	1.7-17.1	
Pore	33	3.4	2.4 - 4.7	2	6.5	1.1 - 19.1	
Mani	21	2.1	1.4 - 3.3	2	9.5	1.6 - 28.1	
Monterrey	21	2.1	1.4 - 3.3	1	4.8	0.2 - 21.3	
Nunchía	20	2.0	1.2 - 3.1	5	20.0	7.1 - 43.3	
Hatocorozal	15	1.5	0.9 - 2.6	2	13.3	2.3 - 37.5	
Orocue	13	1.3	0.7 - 2.3	1	7.7	0.4 - 32.5	
Támara	10	1.0	0.5-1.9	1	10.0	0.5 - 40.4	
Other†	13	1.3	0.7 - 2.3	0	0.0	0.0 - 20.6	
Total	982	100.0		39	4.0	2.8 - 5.3	

^{*} CI = confidence interval.

18 years of age. All results obtained were delivered to the patients and health authorities were officially informed of the results to continue the process of complementary diagnosis. A monitoring program was developed. It included home visits,

clinical evaluation, and laboratory tests (polymerase chain reaction and hemoculture) for parasite-positive women and their newborns from birth and serologic analysis for infants more than eight months of age. Follow-up and administration of etiologic treatment to infected mothers, infants, and siblings was conducted as part of this program.

RESULTS

Study population and descriptive analysis. Of 990 pregnant women who received prenatal care, five were excluded because their samples were inadequate to be processed for laboratory tests, and three were excluded because they resided in other departments different from Casanare. Therefore, 982 patients (99.2%) were included in the analysis. Their age range was 13–46 years. Most had a knowledge of the vector and lived in houses at risk for disease during their childhood. The global prevalence of *T. cruzi* infection in the population studied was 3.97% (95% CI = 2.8–5.3%). Differences were found in *T. cruzi* infection frequencies in the 19 municipalities of residence. Nunchia and Hatocorozal had the highest prevalences, 20% and 13%, respectively (Table 1). The prevalence of infection in women less than 15 years of age was 2.4% (1 of 42).

Associations with *T. cruzi* **infection.** Bivariate analysis showed that the most significant differences between positive

TABLE 2
Socioepidemiologic factors related with *Trypanosoma cruzi* infection in pregnant women, Casanare, Colombia*

Variable	Pregnant women included		Frequency T. cruzi infection				
	No.	%	No.	%	cOR	95% CI	P
Age (years)							
> 25th Percentile (< 19)	195	19.9	3	1.5	Ref.		
25–75th Percentile (19–28)	534	54.4	17	3.2	2.1	0.6 - 7.3	0.00
\geq 75th Percentile (29–46)	253	25.7	19	7.5	4.9	1.4 - 17.0	
Knowledge of vector							
No	430	43.8	10	2.3	Ref.		0.03
Yes	551	56.2	28	5.1	2.2	1.1 - 4.8	
Contact with vector at least once							
No	496	58.5	12	2.4	Ref.		0.03
Yes	352	41.5	24	6.8	2.9	1.4-6.5	
Contact with vector in past year							
No	876	89.8	27	3.1	Ref.		0.00
Yes	99	10.2	11	11.1	3.9	1.8-8.2	
Animals within household							
No	469	47.8	11	2.3	Ref.		0.01
Yes	512	52.2	27	5.3	2.3	1.2 - 4.6	
Socioeconomic stratum†							
II or III	282	37.7	6	2.1	Ref.		0.04
I	693	71.0	33	4.8	2.1	1.0-5.5	
Education level							
University	138	14.1	1	0.7	Ref		0.00
High school completed	256	26.2	6	2.3	3.3	0.7 - 27.4	
High school not completed	322	33.0	9	2.8	3.9	0.6 - 24.2	
Primary school completed	156	16.0	9	5.8	8.4	1.0 - 67.0	
Primary school not completed	104	10.7	13	12.5	19.6	2.5-152.2	
History of Chagas disease in relatives							
No	684	83.9	23	3.4	Ref.		0.08
Yes	131	16.1	9	6.9	2.1	1.0 - 4.7	
Health insurance type							
Contributive	145	14.8	1	0.7	Ref.		0.05
Subsidized	800	81.5	37	4.5	6.8	0.9-50.0	
None	37	3.8	1	2.7	3.9	0.2 - 63.7	
Current residence area							
Urban	673	70.8	16	2.4	Ref.		0.00
Rural	278	29.2	20	7.2	3.2	1.6-6.3	

^{*} cOR = crude odds ratio; CI = confidence interval; Ref. = reference value.

 $[\]dagger\!\leq\!3$ patients each: Sácama (3), Recetor (3), Chámeza (3), Villanueva (2), La Salina (1), and Sabanalarga (1).

[†] According to the Sistema de Identificación de Potenciales Beneficiarios de Programas Sociales, Colombia, 2010.

Table 3
Housing characteristics related with *Trypanosoma cruzi* infection in pregnant women, Casanare, Colombia*

Variable	Pregnant women included		Frequency <i>T. cruzi</i> infection				
	No.	%	No.	%	cOR	95% CI	P
Floor in childhood dwelling							
Cement or tile	472	50.91	8	1.69	Ref.		0.01
Soil	455	47.1	27	5.93	3.7	1.7-8.3	
Roof in childhood dwelling							
Tiles	499	52.2	10	2.0	Ref.		0.00
Thatch	28	2.9	1	3.6	1.8	0.2 - 15.0	
Mud	36	3.8	1	2.8	1.4	0.2 - 11.1	
Palm leaves	274	28.7	21	7.7	3.8	1.8-8.2	
Other	119	12.4	2	1.7	0.8	0.2 - 3.9	
Wall type in childhood dwelling							
Brick/block	378	39.4	5	1.3	Ref.		0.00
Cement	117	12.2	2	1.7	1.3	0.2-6.8	
Bahareque	55	5.7	2	5.7	2.8	0.5–14.9	
Adobe	195	20.1	12	6.2	4.9	1.7–14.1	
Wood	186	19.4	13	7.0	5.6	2.0–16.0	
Other	30	3.1	1	3.3	2.5	0.3–22.0	
Floor in current dwelling							0.01
Cement or tile	865	90.8	28	3.2	Ref.		
Soil	88	9.20	10	11.4	3.8	1.8-8.2	
Roof in current dwelling	00	,.20	10	1111	2.0	1.0 0.2	
Tiles	745	76.8	25	3.4	Ref.		0.16
Thatch	39	0.4	0	0	_	_	0.10
Mud	28	2.9	0	ő	_	_	
Palm leaves	39	4	4	10.3	3.3	1.1-10.0	
Other	154	15.8	8	5.2	1.6	0.7–3.6	
Wall in current dwelling	154	13.0	O	3.2	1.0	0.7 5.0	0.00
Brick/block	655	67.5	22	3.4	Ref.		0.00
Cement	183	18.9	5	2.7	0.8	0.3-2.2	
Bahareque	19	2.0	1	5.3	1.5	0.2–11.8	
Adobe	45	4.6	1	2.2	0.6	0.1–4.9	
Wood	39	4.0	7	17.9	6.3	2.5–15.8	
Other	29	3.0	1	3.4	1.0	0.1–7.9	
Other	29	5.0	1	3.4	1.0	0.1-7.9	

^{*} cOR = crude odds ratio; CI = confidence interval; Ref. = reference value.

and negative patients were found in variables such as age, education level, knowledge of the vector, history of contact with vectors, animals within the household, history of Chagas disease in relatives, type of health insurance, and current residence area (Table 2). The mean \pm SD age was 29.7 \pm 8.5 and 24.1 \pm 6.3 years in infected and non-infected women, respectively.

Two variables (age and education level) showed a doseresponse effect. For age it showed a higher risk in older women. For education, a lower level of education showed a higher risk than a university education.

Housing characteristics were found with significant differences between infected and non-infected pregnant women not

Table 4
Multivariate analysis of associated risk factors for Chagas disease in pregnant women, Casanare, Colombia*

Variable	aOR	95% CI
Age < 19 years	1	
Age 19–28 years	1.6	0.4 - 5.9
Age 29–49 years	3.4	0.9-12.4
Urban residence	1	
Rural residence	2.2	1.0 - 4.6
University	1	
High school completed	2.3	0.2-20.9
High school not completed	3.3	0.4-27.9
Primary school completed	5.5	0.7-45.8
Primary school not completed	10.2	1.6-82.7
No knowledge of vector	1	
Knowledge of the vector	2.2	1.0-4.9

^{*}aOR = adjusted odds ratio; CI = confidence interval.

only during childhood but also when the study was conducted. During childhood, the most important T. cruzi infection–related variables were a soil floor, a palm leaf roof, earth walls, and wooden walls. Likewise, in 2010, the most important associated variables were a soil floor, a palm leaf roof, adobe walls, and wooden wall. The frequency of these risk factors in the population studied was higher when housing conditions during childhood were compared with at the time the study was conducted. For instance, the prevalence of a soil floor was 47.1% (n = 455) in childhood and 9.2% (n = 88) in 2010. Similar findings were obtained when characteristics of roofs and walls were compared (Table 3). The logistic regression model showed that four variables (age, living in a rural area, education level, and knowledge of the vector) were significant (Table 4).

House visits. Of 93 relatives sampled, 9 (9.3%) were positive. The age distribution for infected relatives was 20% for those 0–18 years of age, 40% for those 19–45 years of age, and 20% for those > 46 years of age. The age distribution for non-infected relatives was 54% for those 0–18 years of age, 30% for those 19–45 years of age, and 17% for those > 46 years of age. In addition, it was possible to verify the characteristics of the houses. Insecticide vector control was performed in all houses.

DISCUSSION

Prevention and control of congenital transmission of Chagas disease is one of the major goals of the World Health Organization Chagas disease Control Program; screening of infected pregnant women is important for diagnosing infection and testing their babies.²² In this study, the prevalence and risk factors associated with *T. cruzi* infection in pregnant women in Casanare, Colombia, were studied as a first step to emphasize before health authorities the need to implement a surveillance system for congenital Chagas disease in Colombia.

The observed prevalence of 4.0% is the highest reported until now in pregnant women in Colombia. This prevalence is lower than that reported in disease-endemic regions of Argentina and Bolivia, but higher than those reported in Peru and Brazil. $^{7-9}$

The most relevant T. cruzi infection risk-associated factors were age, knowledge of vector, rural residency and level of education. Similarly, Hidron and others using a multivariate model reported that longer residence in a disease-endemic province, residence in a rural area, and poor housing conditions were associated with T. cruzi infection.²³ In this respect, it is important to highlight that housing characteristics of the pregnant women included in our study were better in 2010, when the study was conducted, than during their childhood. A lower frequency of this risk factor was observed in 2010. This finding could explain the higher prevalence of infection found in older women. Housing conditions have been investigated in Colombia as risk factors associated with the presence of triatomines inside households.²⁴ Although our study explored the association with a different but related outcome (T. cruzi infection), some variables, such as having animals inside the houses, could be related to infections in households.

Education level has an interesting dose-response effect that shows a correlation between the lower level of education and the higher risk for disease. It has been established that education level is an important risk factor related to the prevalence of neglected tropical diseases and, in particular, for Chagas disease. Having subsidized health insurance was found to be an important risk factor by bivariate analysis. This finding is of special importance because in Colombia testing for Chagas disease is not included in this type of health insurance.²⁵ Consequently, this finding indicates that health policy planners should include this testing in insurance coverage. Moreover, Viotti and others found that a low rate of cardiomyopathy progression is associated with more years of education and higher medical insurance coverage.²⁶ These findings are similar to those in our study, which showed that social inequities and socioeconomic problems can increase the likelihood of acquiring diseases.

Few studies have been conducted to determine risk factors for *T. cruzi* infection in pregnant women; most studies focused on congenital cases. Risk factors found in this study constitute an important base for conducting a more specific and direct search for Chagas disease. For regions where Chagas disease is not endemic, it is especially important to investigate possible congenital transmission of Chagas disease among neonates on the basis of age and housing conditions of the mother during her childhood.⁶

Trypanocide drugs are not indicated during pregnancy. For that reason, this study, the etiologic treatment of women after delivery and breastfeeding was implemented as a way to prevent congenital transmission during future pregnancies or complications during chronic disease.²⁷ Likewise, the prevalence of infection in relatives was higher (9.3%) than in pregnant women (4.0%). This finding is consistent with those of

several reports suggesting that screening of Chagas disease in siblings and relatives of infected mothers is an imperative necessity. Home visits represented an important way to find more infected persons.²⁸ This kind of door-to-door investigation has been implemented with great success in identifying congenital cases in Paraguay and Bolivia.^{29,30}

The associated risk factors found are important for conducting a more specific and direct search for Chagas disease. For regions where Chagas disease is not endemic, it is especially important because physicians seldom consider a diagnosis of Chagas disease among their pregnant patients.⁶

In summary, the prevalence results of *T. cruzi* infection in pregnant women point out the importance of implementing a Chagas disease surveillance program in this population as a way to control congenital Chagas disease. Also, the results obtained reflect the prevalence of Chagas disease in young women in a disease-endemic region in Colombia, who could benefit from specific anti-parasitic treatment. Finally, the risk factors associated with *T. cruzi* infection in pregnant women found in this study constitute an important base to design a more specific and directed program for screening for Chagas disease pregnancy.

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